Loss of pten causes tumor initiation following differentiation of murine pluripotent stem cells due to failed repression of nanog.

Journal: PLoS One

Publication Year: 2011

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PubMed link: 21304588

Funding Grants: UCLA CIRM Research Training Program II

Public Summary:
Pluripotent stem cells (PSCs) hold significant promise in regenerative medicine due to their unlimited capacity for self-renewal and potential to differentiate into every cell type in the body. One major barrier to the use of PSCs is their potential risk for tumor initiation following differentiation and transplantation in vivo. In the current study we sought to evaluate the role of the tumor suppressor Pten in murine PSC neoplastic progression. Using eight functional assays that have previously been used to indicate PSC adaptation or transformation, Pten null embryonic stem cells (ESCs) failed to rate as significant in five of them. Instead, our data demonstrate that the loss of Pten causes the emergence of a small number of aggressive, teratoma-initiating embryonic carcinoma cells (ECCs) during differentiation in vitro, while the remaining 90-95% of differentiated cells are non-tumorigenic. Furthermore, our data show that the mechanism by which Pten null ECCs emerge in vitro and cause tumors in vivo is through increased survival and self-renewal, due to failed repression of the transcription factor Nanog.

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